AneuRx stent graft versus open surgical repair of abdominal aortic aneurysms: Multicenter prospective clinical trial

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The results of a prospective, nonrandomized, multicenter clinical trial that compared endovascular stent graft exclusion of abdominal aortic aneurysms with open surgical repair are presented. During an 18-month period, 250 patients with infrarenal aneurysms underwent treatment at 12 study sites—190 patients underwent endovascular repair using the Medtronic AneuRx stent graft (Sunnyvale, Calif), and 60 underwent open surgical repair. There was no significant difference in operative mortality rates between the groups. The patients who underwent stent grafting had significant reductions in blood loss, time to extubation, and days in the intensive care unit and in the hospital, with an earlier return to function. The major morbidity rate was reduced from 23% in the surgery group to 12% ($P < .05$) in the stent graft group. There was no difference in the combined morbidity/mortality rates between the two groups. Primary technical success at the time of discharge for the patients with stent grafts was 77%, largely as a result of a 21% endoleak rate. At 1 month, the endoleak rate had decreased to 9%. There was no difference in the primary or secondary procedure success rates at 30 days between the surgery and stent graft groups. The primary graft patency rate at 6 months was 98% in the surgery group and 97% in the stent graft group. The aneurysm exclusion rate at 1 month and 6 months was 100% in patients who underwent surgery and 91% in patients who underwent stent grafting. Stent graft migration occurred in three patients and resulted in late endoleaks; each endoleak was corrected by means of endovascular placement of a stent graft extender cuff. There have been no aneurysm ruptures and no surgical conversions to open repair in the stent graft group. Stent graft repair compares favorably with open surgical repair, with a reduced morbidity rate, shortened hospital stays, and satisfactory short term outcomes. (J Vasc Surg 1999;29:292-308.)

The natural history of abdominal aortic aneurysms is enlargement and rupture.[1] The prevalence of abdominal aortic aneurysm has increased in the past 30 years,[2] and up to 50% of patients with untreated aneurysms will die of rupture in a 5-year period.[3-5] Open surgical repair is effective in the prevention of rupture and can be performed with 2% to 5% mortality rates in most experiences.[6-9] However, patients with aneurysms are generally elderly and often have significant associated comorbid medical conditions that increase the operative risks. Furthermore, open surgical repair is associated with significant morbidity rates in 15% to 30% of patients.[9,10] Because of the considerable risks associated with open surgical repair of aortic aneurysms, less-invasive treatment options with endoluminal stent grafts are gaining favor.

Endovascular stent graft repair of abdominal aortic aneurysms offers the possibility of reduction of the perioperative risk of aneurysm repair. Since the first endovascular aneurysm exclusion by Parodi et al[11] in 1991, a number of devices and strategies have been developed and evaluated.[12-20] Successful aneurysm exclusion has been achieved in 50% to 90% of cases,[12-20] but a number of problems have been identified, including vessel perforation, the inability to seal the aneurysm, the inability to advance the device

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through the iliac artery, and the need for conversion of the procedure to open surgical repair.[15] Numerous reports describe an ever-increasing number of experiences with endovascular stent grafting of aneurysms, but most lack a surgical control group. Retrospective reviews that compare endoluminal aneurysm repair with concurrent open surgical repair have revealed no differences in perioperative mortality rates and shorter hospital stays with endoluminal repair.[21]

We report the results of a prospective, nonrandomized, multicenter controlled clinical trial that compared open surgical repair with endovascular repair of infrarenal abdominal aortic aneurysms. The clinical trial compared a prospectively defined surgical control group with the initial phase I and phase II clinical experiences with the Medtronic AneuRx stent graft system (Sunnyvale, Calif). Thus, this report includes the learning curve involved with the use of this new endovascular approach for the treatment of aortic aneurysms.

METHODS

Endovascular prosthesis. The Medtronic AneuRx stent graft is a modular bifurcated stent graft system. The modular stent graft components consist of a thin-walled, noncrimped woven polyester graft supported with a nickel-titanium alloy (Nitinol) exoskeleton. The primary components are a main bifurcated segment and a contralateral iliac limb. Additional modular components include aortic and iliac extender cuffs (Fig 1). The components of the self-expanding stent graft are contained in a delivery sheath and are introduced through a retrograde approach with fluoroscopic imaging control through small femoral arteriotomies. The bifurcated device is available in aortic diameter sizes from 20 to 28 mm and iliac diameter sizes from 12 to 16 mm. Length adjustments can be made with proximal and distal extender cuffs.[19-20,22]

Clinical study design. This clinical investigation was undertaken to evaluate the safety and effectiveness of the Medtronic AneuRx stent graft system in the treatment of infrarenal abdominal aortic aneurysms and to compare its safety and effectiveness with the medical standard of care, namely open surgical repair. The study design consisted of a phase I feasibility study (four study sites) to show an adequate level of safety and effectiveness to justify expansion to a phase II controlled study according to Food and Drug Administration guidelines. The phase II clinical study expanded the number of investigational study sites to 12 and compared the stent graft treatment with standard surgical repair. Each study site received approval and oversight from its Institutional Review Board (See Appendix).

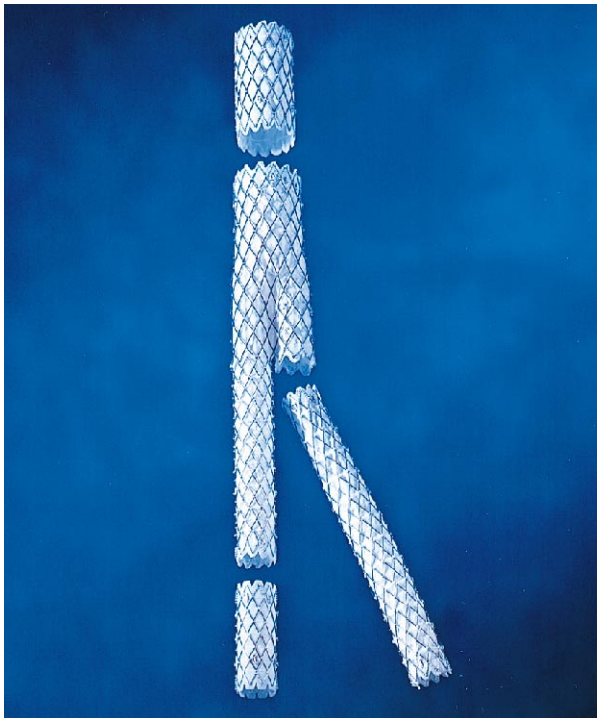

Fig 1. Modular design of AneuRx stent graft system. Primary modular components are main bifurcated segment and contralateral iliac limb. Modular proximal (aortic) and distal (iliac) extender cuffs allow length adjustment.

Patient selection. Patients with nonruptured infrarenal aortic and aortoiliac aneurysms were candidates for the trial if the aneurysm met one of the following criteria: larger than 5 cm in diameter, between 4 and 5 cm in diameter with a documented increase of 0.5 cm in the past 6 months, twice the diameter of the infrarenal neck, or saccular. Additional requirements included an infrarenal neck between 18 and 26 mm in diameter with a minimum length below the most inferior renal artery of 1.0 cm without excessive tortuosity. Iliac artery requirements included a lumen caliber that allowed access with a 21F (outside diameter) delivery catheter on one side and a 16F sheath on the contralateral side with a maximum distal iliac artery diameter of 16 mm.

Exclusion criteria included the following conditions: age less than 18 years; acute renal failure; pregnancy or lactation; connective tissue disease; active systemic infection; hypercoagulability; a traumatic aneurysm; problems that prevented follow-up; life expectancy of less than 1 year; the inability to give informed consent; an acutely ruptured or leak-

ing aneurysm; a suprarenal, thoracic, or inflammatory aneurysm; and morbid obesity that limited x-ray imaging capability.

Before entering the study, each patient underwent evaluation with a contrast-infused computed tomographic (CT) scan and contrast angiography to evaluate the morphologic features of the aneurysm and visceral branch vessels. Some patients also underwent magnetic resonance angiography and intravascular ultrasound scan imaging, particularly in the cases in which limitation of contrast infusion was indicated. All the patients were operative candidates, with American Society of Anesthesiologists (ASA) risk classifications I to IV, signed informed consent, and agreements to 1-year follow-up periods.

Surgical controls. Patients and referring doctors often decline open surgical repair if endovascular repair is a treatment option, which could potentially result in unmatched treatment groups. Therefore, in an effort to match the surgical and endovascular study groups, the patients for surgical control were prospectively enrolled at each of the 12 study sites before the enrollment of the patients in the endovascular treatment group. The entry criteria were the same for the patients for surgical control and the patients for stent grafting. The patients who met the study inclusion and exclusion criteria underwent aortic imaging procedures. Those who met the study criteria for stent graft repair were provided with informed consent and were invited to participate in the study. Those patients who signed the informed consent and agreed to the follow-up protocol were accepted into the surgical control group and underwent open surgical repair. After the surgeons at a study site had operated on five patients for surgical control, the site was authorized to begin endovascular stent graft treatment with the same patient entry criteria. Follow-up was required at the same intervals for both the surgical and stent graft groups and was continued for at least 1 year.

Surgical and endovascular treatment procedure. The patients in the surgical control group underwent operative repair of the aneurysm with general anesthesia and with standard open surgical techniques. Either a transperitoneal or a retroperitoneal approach was used to expose the aneurysm, and a prosthetic tube or bifurcated graft was sutured in place to exclude the aneurysm. The endovascular stent graft procedures were performed in the operating room or the endovascular procedure room with general or epidural anesthesia and femoral artery exposure through groin incisions. A team approach with a vascular surgeon and an interventional radiologist working together was used. The intraoperative imaging was performed with fixed or portable fluoroscopy, intraoperative angiography, and intravascular ultrasound scanning. All 250 patients in the two arms of the study underwent treatment during an 18-month period that began in May 1996 and ended in November 1997.

Follow-up evaluation. Before hospital discharge, abdominal x-rays and spiral CT angiography were performed in patients with stent grafts to document the position and patency of the stent graft and to evaluate aneurysm size, branch vessel patency, and the presence or absence of contrast fill of the aneurysm, or endoleak (Fig 2). All the imaging studies were evaluated locally at each study site and at an independent central core laboratory. After hospital discharge, all the patients in both the surgical and stent graft groups were evaluated at 1 month, 6 months, and 1 year. The patients with stent grafts underwent imaging with color duplex ultrasound scan or contrast CT scan at 1 month and contrast CT imaging at 6 and 12 months (Fig 3).

Statistical analysis. The results are expressed as the mean ± the standard deviation. Differences between the groups were evaluated with χ^2 test and two-tailed Student *t* test. Differences were reported as significant if the *P* value was less than .05.

RESULTS

Phase I stent graft feasibility trial. Phase I of the trial included 40 patients with infrarenal abdominal aortic aneurysms (5.7 ± 0.8 cm) who underwent treatment at four study centers. The AneuRx stent graft was successfully deployed in all 40 patients, with successful exclusion of the aneurysm. There were no endoleaks and no surgical conversions. Three patients (7.5%) died in the 30-day perioperative period—two from chronic obstructive pulmonary disease and respiratory failure, and one from sepsis as a result of a gangrenous gallbladder. There were four major complications (10%): two patients had iliac limb thrombosis and required femoral-femoral bypass grafting, one patient required common femoral endarterectomy for focal stenosis, and one patient had cardiac arrhythmia. There were no device related deaths and no aneurysm ruptures or late surgical conversions.

Phase II clinical trial. Phase II of the trial included 150 patients who underwent treatment with the stent graft system at 12 study centers. The initial experience with the endovascular procedure in eight study centers occurred during phase II. The number of patients who underwent treatment at each center ranged from 1 to 26, with a mean of 13.

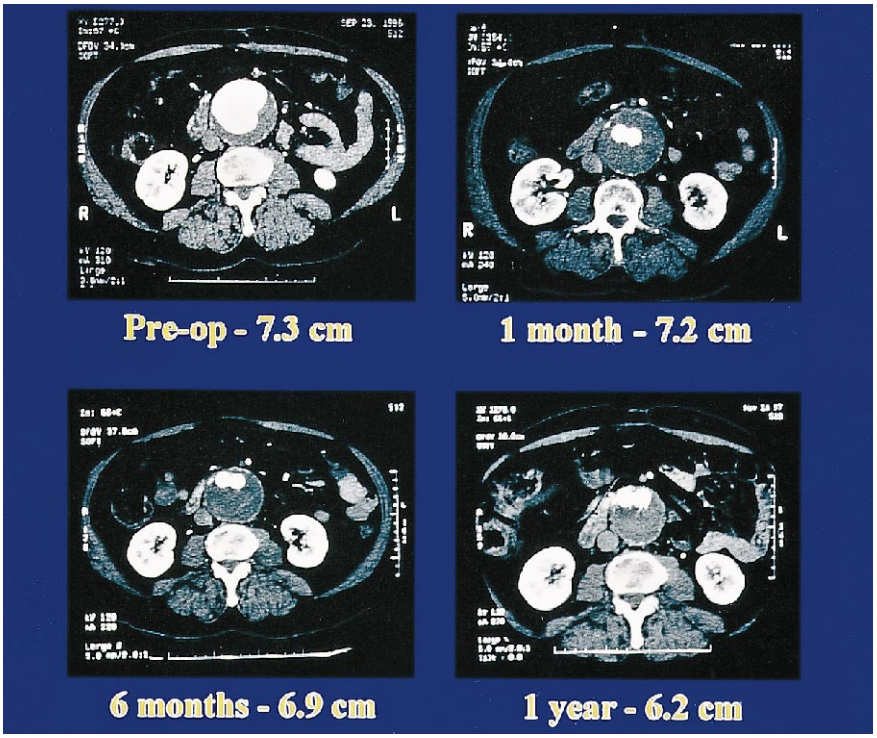

Fig 2. Cross-sectional images of contrast infused spiral computed tomographic scans of 67-year-old man with 7.3-cm abdominal aortic aneurysm. **A,** Preoperative computed tomographic scan shows 7.3-cm abdominal aortic aneurysm with little mural thrombus. **B,** One month after stent graft placement, aneurysm is fully excluded with no endoleak and no change in aneurysm size. **C,** After 6 months, aneurysm has decreased in size to 6.9 cm. **D,** After 1 year, aneurysm has decreased in size to 6.2 cm.

There was no difference in outcome between the three centers that contributed the largest number of patients (40% of the total) and the remaining nine centers. The periprocedural (30-day) mortality rate was lower (2 of 150, 1.3%) in phase II than in phase I (3 of 40, 7.5%; $P < .05$). Procedure time, blood loss, and intensive care unit (ICU) time were lower in phase II than in phase I ($P < .01$), which reflects improvements in the stent graft procedure gained during phase I. There were no other significant differences between the two phases of the trial. Therefore, the results of phase I and phase II endovascular treatment groups are combined as the stent graft group. The first 190 patients who underwent treatment in the United States with the AneuRx stent graft system, including the initial learning curve at each site, are thus compared with the 60 patients who underwent treatment with open surgery to comprise this report.

Patient characteristics. The characteristics of the patient populations for surgery and stent grafting are listed in Table I. Patients in both groups had multiple risk factors and comorbidities, but there were no significant differences between the groups. The ASA operative risk classification tended to be higher in the patients for stent grafts, with 26% in ASA IV and 9% in ASA I and II, as compared with the surgery group, which had 17% in ASA IV and 18% in ASA I and II. However, these differences were not statistically significant ($P = .07$). There was no difference in aneurysm size between the surgery and stent graft groups, and all the patients met the morphologic entry criteria for stent grafting.

Primary procedure results. Open surgical repair of the abdominal aortic aneurysm was successfully accomplished in all 60 patients for surgery (100%). The stent graft was successfully deployed in 185 of 190 patients for stent grafts (97%; Table II). In four patients for stent grafts, the aorta could not be accessed through the iliac artery and the procedure was terminated. These four patients declined open surgical repair and returned to their referring

Table I. Patient characteristics

Risk factors/comorbidities	*Surgery (n = 60)*	*Stent grafting (n = 190)*	*P value*
Mean age (years)	69 ± 7	73 ± 8	NS
Age range (years)	49 to 97	45 to 91	NS
Male gender	85%	90%	NS
Family history of AAA	15%	8%	NS
Smoking	83%	85%	NS
COPD	33%	23%	NS
Hypertension	60%	69%	NS
Coronary artery disease	87%	84%	NS
History of MI	25%	34%	NS
CABG/PTCA	55%	45%	NS
Stroke/TIA	15%	19%	NS
Peripheral vascular disease	25%	18%	NS
Diabetes mellitus	10%	7%	NS
Renal failure	5%	4%	NS
Obesity	15%	21%	NS
Alcohol use	5%	5%	NS
Carcinoma	23%	21%	NS
ASA risk category			
I to II	18%	9%	
III	65%	65%	
IV	17%	26%	NS ($P = .07$)
Aneurysm size (cm)	*5.6 ± 1.1*	*5.6 ± 0.9*	*NS*
Range of size (cm)	3.5 to 10.0	3.3 to 9.0	NS

AAA, Abdominal aortic aneurysms; *COPD,* chronic obstructive pulmonary disease; *MI,* myocardial infarction; *CABG,* coronary artery bypass grafting; *PTCA,* percutaneous transluminal coronary angioplasty; *TIA,* transient ischemic attack; *ASA,* American Society of Anesthesiologists.

physician after a 30-day follow-up period. One patient for stent graft had a myocardial infarction on induction of anesthesia. The procedure was cancelled, and the patient has declined a subsequent procedure. There were no surgical conversions to open aneurysm repair in the stent graft group, and no patient has had a ruptured aneurysm.

There was no difference in anesthesia time or procedure time between the two groups. The patients who underwent treatment with stent grafts had 60% less blood loss as compared with the patients who underwent open surgery ($P < .001$), and these patients required 80% less blood transfusions ($P < .05$). The blood loss in the patients for stent grafts was primarily caused by leakage from catheters, sheaths, and hemostatic values. Only 12% of the patients in the stent graft group underwent a blood transfusion as compared with 40% in the surgery group ($P < .001$). There was a marked reduction in the time to extubation, discharge from the ICU, ambulation without assistance, and eating a regular diet in the stent graft group as compared with the surgery group (Table II). The hospital length of stay was reduced by two thirds in the stent graft group, from 9.4 days to 3.4 days ($P < .001$).

Mortality rates. All the patients survived open surgical repair; the operative mortality rate in the surgery group was 0%. Five patients (2.6%) died in the stent graft group. There was no significant difference in the mortality rates between the two groups (Table III). Three of the 40 patients in phase I died during the 30-day perioperative period—two from chronic obstructive pulmonary disease and respiratory failure, and one from sepsis as a result of a gangrenous gallbladder. Two of the 150 patients in phase II died during the 30-day perioperative period: one from colon ischemia and multisystem organ failure, and one as a result of myocardial infarction. The mortality rate was significantly lower in phase II (1.3%) as compared with phase I (7.5%; $P < .05$). The youngest patient in the study was in phase II. This patient was 45 years old, had no cardiac symptoms, and had negative preoperative, noninvasive evaluation results by a cardiologist. The patient was discharged 3 days after successful stent graft repair. Twenty days later, the patient had a myocardial infarction, underwent coronary angiography, and was discovered to have a 95% left main coronary stenosis—he died during interventional efforts to

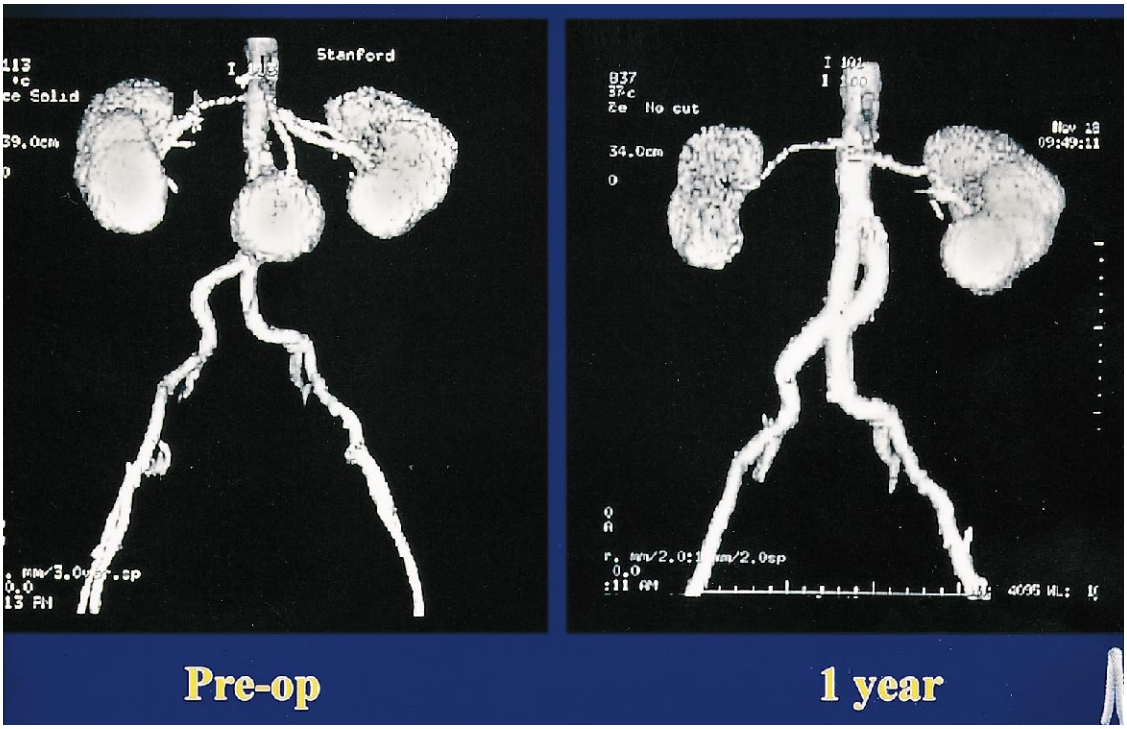

Fig 3. Shaded surface of three-dimensional reconstruction of spiral computed tomographic scan showing: **A,** a 6.2-cm infrarenal aortic aneurysm in a 65-year-old man; and **B,** 1 year later, complete exclusion of aneurysm by stent graft. Aneurysm has decreased in size to 5.2 cm (not seen in this image).

Table II. Primary procedure results

	Surgery (n = 60)	*Stent grafting (n = 190)*	*P value*
Procedure success rate	100%	97%	NS
Anesthesia time (hours)	4.9 ± 1.8	4.5 ± 1.6	NS
Procedure time (hours)	3.6 ± 1.6	3.1 ± 1.3	NS
Blood loss (mL)	1596 ± 1432	641 ± 636.	<.001
Blood replaced (units)	1.6 ± 3.8	0.3 ± 1.2	<.05
Patients requiring transfusion	40%	12%	<.001
Extubation time (days)	0.9 ± 2.3	0.1 ± 0.3	<.05
ICU days	2.5 ± 3.1	0.9 ± 1.2	<.05
Ambulate without assistance (days)	4.0 ± 4.8	1.5 ± 1.2	<.001
Regular diet (days)	5.1 ± 2.5	1.4 ± 0.9	<.001
Hospital days (LOS)	9.4 ± 10.8	3.4 ± 2.7	<.001
Hospital days (range)	3 to 72	1 to 20	

ICU, Intensive care unit; *LOS,* length of stay.

treat the coronary lesion. The oldest patient in the study, who was 97 years old, underwent open surgery, had no complications and was alive and well 1 year later.

Morbidity rates. Complications were markedly reduced in the stent graft group as compared with the surgery group. *Major morbidity* was defined as any condition that necessitated a reoperation or a secondary treatment procedure in the operating room or angiography suite, myocardial infarction, major arrhythmia, stroke, renal failure that necessitated dialysis, or another medical condition that prolonged hospital stay more than 7 days in the surgery group or more than 5 days in the stent graft group. Major morbidity occurred in 23% of the patients who underwent open surgery, whereas only 12% of

Table III. Mortality and morbidity rates (30 days)*

	Surgery (n = 60)		*Stent grafting (n = 190)*		
	Patients	*%*	*Patients*	*%*	*P value*
Mortality	0	0	5	3	NS
Device-related mortality	0	0	0	0	NS
Major morbidity	14	23	22	12	<.05
Surgical complications	7	12	16	9	NS
Medical complications	7	12	6	3	<.01
Minor morbidity	4	7	10	5	NS

*Each patient was counted once with the most severe event recorded.

the patients who underwent stent grafting had a major complication ($P = .03$; Table III). Major morbidity included surgical and medical complications. The surgical complications included the need for reoperation in 12% of the patients who underwent open aneurysm repair, with 5% needing more than one reoperation. Of the patients who underwent stent graft repair, 9% had reoperations or secondary procedures and none needed more than one reoperation. Major medical complications were more common in the surgery group (12%) as compared with the stent graft group (3%; $P = .009$).

Minor morbidity was defined as complicating events that did not prolong hospital stay greater than 7 days in the surgery group or greater than 5 days in the stent graft group. This included, in the surgery group, two patients with leg numbness and weakness, one patient with pneumonia, and one patient with a urinary tract infection. In the stent graft group, this included two patients with superficial groin wound infections, two patients with minor toe embolizations that did not necessitate treatment, one patient with femoral neuropathy, one patient with atrial fibrillation, and three patients with mildly elevated creatinine levels. There was no difference in minor morbidity rates between the two groups (Table III).

Combined morbidity/mortality rates. The major morbidity/mortality rate in the open surgery group (23%) was not statistically different from that of the stent graft group (14%). The total morbidity/mortality rate in the open surgery group (30%) was not significantly different from that of the stent graft group (19%).

Major morbidity. The major complications are summarized in Table IV. There was no difference between the two groups in the number of patients with complications that necessitated reoperation. However, there was a significant difference in the magnitude of the complications between the two groups. In the surgery group, six patients (10%) required major abdominal operations—two for colon ischemia, two for postoperative bleeding, one for wound dehiscence, and one for infection. Three of the six patients required more than one major reoperation. In the stent graft group, two patients (1%) required abdominal operation—one for colon ischemia as a result of inferior mesenteric artery (IMA) and internal iliac occlusion, and one for bleeding as a result of a guide wire that was introduced through the brachial artery and perforated a superior mesenteric artery branch. This difference was highly significant ($P < .001$). There was no difference between the groups in the requirement for groin or peripheral reoperation. One patient in the surgery group underwent thrombectomy for graft limb thrombosis. In the stent graft group, four patients required reoperation to repair endoleaks, two patients to correct graft limb thrombosis, three patients to correct femoral artery stenosis, two patients to repair femoral artery occlusion, one patient to repair a brachial arteriovenous fistula, and one patient to release an entrapped femoral cutaneous nerve. One patient in the stent graft group fell and sustained a hip fracture, which necessitated surgical pinning. The mean hospital length of stay in the patients for surgery who required reoperations was prolonged considerably to 31 days ($P < .05$), whereas the mean hospital stay in the patients with stent grafts who required reoperation was only prolonged to 7 days, which was no different from the mean length of stay of the patients for surgery.

Medical complications were more frequent in the surgery group as compared with the stent graft group ($P < .01$). The patients with major complications had a significant increase in hospital length of stay in both the surgery and the stent graft groups as compared with those patients without complications

Table IV. Major complications*

	Surgery (n = 60)		*Stent grafting (n = 190)*		
	Patients	*%*	*Patients*	*%*	*P value*
Surgical complications	7	12	16	9	NS
Major abdominal	6	10	2	1	<.001
Groin/peripheral	1	2	13	7	NS
Other	—	—	1	1	NS
Hospital LOS (days)	31 ± 22		7 ± 7		<.05
Medical complications	7	12	6	3	<.01
MI/arrhythmia	3	5	4	2	NS
CVA	2	3	1	1	NS
Other	2	3	1	1	NS
Hospital LOS (days)	11 ± 7		9 ± 6		NS
Hospital LOS with complications (days)	21 ± 18		8 ± 7		<.05
Hospital LOS without complications (days)	6 ± 2		3 ± 2		<.001

*Each patient counted once with most severe event recorded.
LOS, Length of stay; *MI,* myocardial infarction; *CVA,* cardiovascular accident.

Table V. Procedure success

	Surgery (n = 60)		*Stent graft (n = 190)*		
	Patients	*%*	*Patients*	*%*	*P value*
Primary technical success*	59	98	146	77	<.01
Primary procedural success†	46	77	148	78	NS
Secondary procedural success‡	57	95	169	89	NS
Aneurysm excluded at 30 days	60	100	164	91	<.05

*No death with complete exclusion of the aneurysm with patent graft at discharge.
†Patient alive, aneurysm excluded, graft patent, no major morbidity or secondary procedure at 30 days.
‡Patient alive, home from hospital, aneurysm excluded, graft patent at 30 days.

(Table IV). The hospital length of stay in the surgery group was at least twice as long as in the stent graft group, whether or not there was a complication.

Procedural success rate. *Primary technical success* was defined in accord with the Society for Vascular Surgery and the International Society for Cardiovascular Surgery (SVS/ISCVS) reporting standards for lower extremity arterial endovascular procedures[24] and adapted for endovascular aortic aneurysm repair. Primary technical success was on the basis of intent to treat and included all patients who consented to enter either the surgical or stent graft group. The patients who survived the procedure and had an excluded aneurysm with a patent graft without significant kinks, twists, or obstruction at the time of discharge and without need for a secondary procedure were considered to be primary technical successes. The primary technical success rate in the surgery group was 98%. One patient had a graft limb thrombosis and required thrombectomy. The primary technical success rate in the stent graft group was 77% ($P < .01$). Five patients died, and 39 had endoleaks on CT scan at 24 to 48 hours (Table V). However, the SVS/ISCVS reporting guidelines do not fully take into consideration the complications that may accompany surgical and stent graft procedures. Therefore, a primary procedure success rate was defined.

Primary procedural success was defined as patients who were alive at 30 days with a patent graft, excluded aneurysm (no endoleak), no need for reoperation or secondary procedure, and no major complication. Primary procedural success in the surgery group was 77% (46 of 60 patients) and in the stent graft group was 78% (148 of 190 patients). There was no difference in the primary procedural success rate between the two groups (Table V).

Secondary procedural success was defined as patients who were alive and home from the hospital at 30 days with an excluded aneurysm and a patent

Table VI. Adverse events related to stent graft procedure

	Patients	*%*
Failure to access iliac artery	4	2
Iliac artery dissection	4	2
Embolization, major	0	0
Embolization, minor	3	2
Unintentional branch occlusion (6 internal iliac, 1 renal)	7	4
Colon ischemia	2	1
Creatinine >2.0 (no dialysis)	7	4
Femoral artery repair	6	3
Femoral neuropathy	2	1
Iliac limb thrombosis	5	3

Table VII*A*. Endoleaks after stent graft repair

Time of evaluation	*Number of endoleaks*	*%*
Before discharge	39/185	21
1 month after procedure	16/180	9
6 months after procedure	15/167	9
12 months after procedure	2/33*	6

*Two endoleaks at 12 months (one, aneurysm size has decreased from 6.5 to 5.0 cm; one, sealed at 15 months).

Table VII*B*. Secondary procedures for endoleaks (11/185 = 6%)

Procedure	*No.*	*Time after stent graft*
Proximal extender cuff	5	Three before discharge One at 8 months One at 12 months
Distal extender cuff	5	Three before discharge One at 2 months One at 12 months
Lumbar artery coiling	1	One at 1 month
Total	11	

graft. This measure of success excludes complications and includes the benefits of secondary procedures. Secondary procedural success in the surgery group was 95%; three patients were still in the hospital as a result of complications. Secondary procedural success in the stent graft group was 89%; five patients had died, and 16 had endoleaks. There was no statistical difference in the secondary procedural success rate between the groups.

The aneurysm exclusion rate at 30 days in surviving patients who had undergone stent graft placement was 91%. There were 180 surviving patients with stent grafts, and 16 had endoleaks at 1 month. The aneurysm exclusion rate in patients who underwent treatmentd with open surgery was 100%.

Stent graft procedure—adverse events. Adverse events that were related to the stent graft procedure are summarized in Table VI. Failure to gain 21F delivery catheter or 22F access sheath to the aorta through the iliac artery occurred in four patients (2%) and resulted in abandoning the stent graft procedure. External iliac artery dissection occurred in four patients (2%) as a result of sheath advancement and necessitated repair during the primary procedure with an uncovered stent, endarterectomy, or an interposition vascular graft. There has been no limb ischemia as a result of this occurrence. Minor embolization was noted in three patients: two patients had evidence of embolization to the toes with no tissue loss and no intervention, and one patient was noted to have a segmental renal infarct on postoperative CT scan. There has been no major embolization that necessitated treatment. Branch vessel occlusion occurred in nine patients; eight internal iliac arteries and one renal artery. Two internal iliac arteries were intentionally occluded because of internal iliac aneurysm, and six internal iliac arteries were unintentionally occluded. Most of these patients had mild, transient hip and buttock claudication that was not disabling. One renal artery was occluded with a proximal extender cuff. This patient is asymptomatic and normotensive and has a normal creatinine level. Colon ischemia has occurred in two patients: one patient had internal iliac occlusion and died of colon ischemia and multisystem organ failure, and the other had transient but prolonged intraoperative internal iliac obstruction while the introducer sheath was in place and had mild postoperative hematochezia that necessitated supportive treatment only with full recovery. Transient creatinine level elevation greater than 2.0 mg/dL occurred in seven patients (4%). All seven patients recovered, and none have required dialysis. Six patients (3%) have required subsequent groin procedures to correct femoral artery occlusion or stenosis. Two patients had femoral neuropathy, one of whom required groin wound exploration and release of nerve entrapment caused by a suture used to close the groin incision.

Graft patency. Graft limb thrombosis has occurred in five patients (3%) with stent grafts and in one patient (2%) for surgery. Four patients with stent graft have undergone femoral-femoral bypass grafting: two procedures occurred early in phase I in the periprocedural period, one occurred at 2 months, and one occurred at 6 months (Table VI). One patient with stent graft underwent graft limb thrombectomy at 3 months, and one patient for surgery underwent graft limb thrombectomy in the periprocedure period. There has been no limb loss related to graft limb

thrombosis. One patient with stent graft who had a diabetic foot infection has undergone above-knee amputation with a patent stent graft during the follow-up period. The primary stent graft patency rate at 6 months is 97%, and the primary surgical graft patency rate at 6 months is 98%. There is no difference between the groups in graft patency rate.

Endoleaks. Immediately after stent graft deployment, intraoperative angiograms were performed to assess aneurysm exclusion. Endoleaks were reported in only 6% of the completion angiograms, and this study was not believed to be a reliable measure of the endoleak rate. All the patients in the stent graft group underwent contrast infused CT scanning before discharge (usually at 24 to 48 hours) to document the presence or the absence of an endoleak (Table VII). The presence or the absence of contrast within the aneurysm sac was recorded, and the source of the endoleak was localized when possible. Note was made of proximal or distal attachment site endoleaks, graft junction endoleaks, and lumbar or IMA branch flows. A blush of contrast in the aneurysm sac with no identifiable source was classified as "transgraft flow." Endoleaks were identified in 39 of 185 patients (21%) before hospital discharge. Of these, 10 were classified as "transgraft flow" and all were sealed at 1 month. Twelve were felt to be results of lumbar artery/IMA branch flow. Of these, six were sealed at 1 month. One lumbar artery was coiled, which resulted in the sealing of the aneurysm. The remaining five continue to have a persisting endoleak at 6 months. In seven patients, endoleaks were identified at the proximal aortic sealing point. Three patients were returned to the operating room for the placement of a proximal extender cuff. The four patients who were followed had a sealed aneurysm at 6 months. However, two patients returned at 8 and 12 months with recurrence of the proximal endoleaks. These two patients also had evidence of minor graft migration and each underwent placement of a proximal extender cuff with immediate sealing of the aneurysm. In 10 patients, the predischarge endoleak arose from the iliac limb either at its junction to the main bifurcation stent body or at the distal end. Three patients underwent treated with iliac extender cuffs before discharge, and one patient underwent treatment at 2 months with prompt sealing of the aneurysm. Of the seven endoleaks that were observed, five sealed at 1 month and two sealed at 2 and 5 months.

The endoleak rate at 1 month and at 6 months was 9%. Of the 15 aneurysms with an endoleak at 6 months, nine are unchanged in size and five have decreased in size. All 14 patients are clinically well and asymptomatic. One patient with an endoleak at 6 months has an aneurysm that has increased in size from 5 to 6.5 cm. He has multiple medical problems, with urinary tract sepsis and multisystem organ failure, and is judged to be too ill to undergo further evaluation. His aneurysm, though enlarged, remains asymptomatic at 7 months.

At 12 months, two of 33 patients (6%) had an endoleak documented on contrast spiral CT scanning. In one patient, the aneurysm had decreased in size from 6.5 to 5 cm. The other patient had no change in the size of the aneurysm, and the small endoleak has subsequently completely sealed at 15 months. There have been no aneurysm ruptures and no surgical conversions among the 190 patients with stent grafts.

Stent graft migration. In three patients, migration of the stent graft has been identified during the 1-year follow-up period. Each migration has been less than a 1-cm displacement, and each has resulted in the appearance of an endoleak and has been described previously in the endoleak section. Two migrations have occurred in the proximal neck at 8 and 12 months and have been corrected with a proximal extender cuff. Both migrations had low placement of the stent graft in the infrarenal neck at the original procedure and probably could have been prevented with a proximal extender cuff at the time of the original procedure. The third migration resulted in the appearance of endoleak at the iliac junction at 12 months and has been corrected with an iliac extender cuff. The iliac limb had been placed low in the junction segment of the main bifurcation module during the original procedure in a patient with a tortuous iliac artery. A higher placement in the junction gate during the original procedure might have prevented this occurrence.

Late mortality. Two patients (3%) in the surgery group and 8 patients (4%) in the stent graft group have died during the 1-year follow-up period. The two deaths in the surgery group were caused by myocardial infarction at 6 and 10 months. Four late deaths occurred in patients in phase I—two as a result of myocardial infarction at 3 and 6 months, and two as a result of congestive heart failure at 8 and 11 months. Four late deaths occurred in patients with stent grafts in phase II. Two of these deaths were caused by myocardial infarction, one was caused by lung cancer, and one was caused by complications of colon cancer. There have been no aneurysm-related deaths and no stent graft device–related deaths.

DISCUSSION

This prospective clinical trial compared the results of endovascular stent graft repair of abdomi-

nal aortic aneurysms with standard open surgery. Patients in the surgical control group met all the criteria for the stent graft trial and were prospectively entered into the study before the initiation of endovascular stent graft treatments in an effort to prevent selection bias. There were no significant differences between the groups in age, risk factors, comorbidities, or aneurysm characteristics. However, during the course of the study, as the availability of the endovascular stent grafting became known, some patients were referred by physicians for stent grafting because they were considered to be too high risk for open surgery. No additional patients were entered into the surgical control group during the course of the study. In particular, there were no patients in the surgery group who were referred because they were considered to be too high risk for surgery. Thus, if there is an imbalance in the composition of the two study groups, it would be in the direction of patients at higher risk being in the stent graft group and potentially skewing the results in favor of surgery. Although the stent graft group tended to be somewhat older, there were no statistically significant differences between the groups and adverse selection did not appear to significantly influence the results.

The outcome of surgical repair of abdominal aortic aneurysms is usually assessed primarily in terms of perioperative mortality rates. The mortality rates for the surgical repair of nonruptured aneurysms are lowest in recent large, single center reports and range from 0% to 4%,[6-9,25] with a mean of 2%. Multicenter reports generally have somewhat higher mortality rates that range from 3% to 5%,[26-28,30] with a mean of 4%,[31] and population-based reports have a mortality rate of approximately 7%.[5,23,29,32] The mortality rate in this prospective multicenter study was 0% in the surgery group and 2.6% in the stent graft group. Both rates are well within the standard of care and below the mean operative mortality rate (4%) for recent multicenter reports on open surgical repair[31] and below the operative mortality rate (5.6%) reported in concurrent surgical/endoluminal series.[21] Most of the deaths in the stent graft group (7.5%) occurred in phase I, and there was a significant reduction in mortality rate ($P < .05$) in phase II (1.3%), which perhaps was related to improvements in the technical aspects of the procedure as reflected in a significant reduction of operative time and blood loss in phase II as compared with phase I. There was no significant difference in late mortality rates between the two groups, and no deaths could be attributed to the stent graft device.

Mortality rates, however, do not fully characterize the debility that can result from the surgical repair of aortic aneurysms. Complications that prolong hospital stay occur in 15% to 30% of patients who undergo open surgery[9,10] and were seen in 23% of the patients in the surgical control group in this study. Although complications also occurred in the stent graft group, their frequency was reduced by one half when compared with the surgery group. The complication rate in the surgical group in this study is higher than that experienced in some institutions with open aneurysm repair. This is consistent with the observation that multi-institutional trials report a higher complication rate than reported by single centers.[31] This difference was seen in the prospective symptomatic[33] and asymptomatic[34] carotid artery trials in which stroke/death rates were higher than the rates reported in most published series of carotid endarterectomy[35] and highlights the importance of comparison to a suitable control group.

Perhaps more important than the complication rate was the striking reduction in the magnitude of the complications experienced in the stent graft group. Patients with stent grafts who required reoperations generally had relatively minor procedures that were confined to the groin incision, and the hospital length of stay in patients with stent grafts with complications was no different from that of patients for surgery without complications.

Thus, the major proposed advantages of this minimally invasive endovascular approach to aneurysm repair were realized. The stent graft procedure itself was less stressful to the patient than open surgery, with far less blood loss, less need for blood transfusion, earlier extubation, shorter ICU stays, earlier ambulation, and earlier resumption of a regular diet. The hospital length of stay was reduced by two thirds, and patients were able to resume normal function shortly after discharge. Furthermore, there was a marked reduction in major complication rates, especially in the need for major abdominal reoperations, which were associated with the greatest morbidity rates, ICU stays, hospital lengths of stay, and costs. Although cost comparison between open surgical repair and stent graft repair was not a part of this investigation, it is possible that the reduction in complication rates, ICU stay, the number and magnitude of reoperations, and the length of hospital stay that occurred in the stent graft group may result in significant cost savings over open surgical repair.

The primary disadvantages of stent graft repair are twofold. First, not all patients with infrarenal aneurysms are candidates for the procedure.

Although open surgical repair can readily accommodate patients with short or absent infrarenal necks, severe tortuosity, accessory renal arteries, iliac aneurysms and occlusions, and associated branch vessel stenoses, these morphologic features may exclude patients from stent graft repair. Thus, precise preoperative imaging is essential in the selection of patients for the procedure. On the other hand, some patients who are morphologically suited for stent grafting and previously were denied surgical repair because of high medical risk may become candidates for aneurysm repair with a stent graft.

The second and major disadvantage of stent grafting is the uncertainty of the permanence of aneurysm exclusion from the circulation. Continued blood flow in the aneurysm sac (endoleak) exposes the patient to an ongoing risk of aneurysm rupture. Several authors have reported deaths from ruptured aneurysms in patients who had previously undergone stent graft placement.[36,37] However, the true significance of endoleaks and whether the natural history of aortic aneurysms is changed after endoluminal grafting is not yet known. Endoleaks can occur early as a result of inadequate sealing of the stent graft to the aortic neck or iliac arteries, flow through the graft, defects in the graft fabric, or iliac or IMA branch flow. Late leaks can occur from graft migration or change in morphologic characteristics and tortuosity of the aneurysm, aortic neck, or iliac arteries. Continued close surveillance of patients with stent grafts is necessary with repeated imaging procedures. The modular extender cuffs available with the AneuRx stent graft system allows subsequent procedures to correct endoleaks at junction and sealing points both early and late. The early (predischarge) endoleak rate was 21%, and the endoleak rate at 1 and 6 months in this study was 9%. Three new endoleaks between 6 and 12 months necessitated secondary treatments with extender cuffs. The significance of an endoleak and branch vessel flow in an aneurysm that is decreasing in size is unknown.

Stent graft repair of aneuryms is associated with a number of adverse events related to iliac artery access by the large introducer sheath and the occasional need to repair the common femoral artery at the site of introduction of the sheath. This problem is common to all current stent graft devices. Major embolization, reported by others,[37] was not seen in this study. Three patients had minor embolization that did not necessitate treatment: one to the kidney was noted on follow-up CT scan, and two cases of transient discoloration of the toes were documented. Improvements in interventional technique and sheath design likely account for the infrequent occurrence of embolization.

Primary in-hospital technical success was defined in accord with the SVS/ISCVS recommended reporting standards for endovascular procedures.[24] Complete exclusion of the aneurysm from the circulation with no death occurred in 77% of the 190 patients entered into the stent graft trial. This is similar to the 85% primary success rate (intention to treat not specified, one death in the series) reported by Blum et al[18] using the Mialhe Stentor/Vanguard (Boston Scientific, Nattick, Mass) endoprosthesis and higher than the 48% primary technical success rate (46 patients, seven surgical conversions, 17 endoleaks) reported in the Endovascular Technologies (EVT) phase I controlled clinical trial.[12] However, primary technical success does not take into consideration major complication rates, which are prominent in the open surgical repair of aortic aneurysms. To better compare the results of endovascular repair with open surgical repair, we considered the major complication rate and defined primary 30-day procedural success. There was no difference in primary procedural success between surgery (77%) and stent grafting (78%). Secondary procedural success at 30 days considered the benefit of secondary treatments in excluding the aneurysm and did not count complications that resolved and allowed discharge from the hospital in 30 days. The secondary procedural success was 95% in surgery and 89% in stent grafting, which was not statistically different. Endoleaks have been reported in 14% to 44% of patients with a variety of stent graft devices.[13,16-18,37-40] The 1-month endoleak rate of 9% in this series appears to be lower; however, direct comparison trials of various endovascular devices have not been performed. The small number of patients (33) who were observed at 1 year in this series does not allow reliable assessment of the true long-term endoleak rate or long-term outcome.

Surgical conversion has been reported in 2% to 16%[13,16,19,41] of patients who undergo stent graft repair. No patient in this series of endovascular stent graft repair was converted to open repair. If the four patients in whom iliac access was not possible had undergone open repair, the surgical conversion rate would have been 2%.

Longitudinal columar support and a flexible endograft structure are provided by the AneuRx stent graft device. This may account for the absence of apparent longitudinal displacement in this series. Changes in aortic endograft configuration have been noted as the aneurysm morphology changes over

time related to shrinkage of the aneurysm.[42] For this reason, longitudinal columar support combined with a flexible endograft structure may be needed to best accommodate to morphologic changes over time and yet maintain fixation of the device. There was no evidence of kinking of the endograft in association with the longitudinal shrinkage of the aneurysm in our patient series. In this study, three patients had mild lateral displacement and reappearance of late endoleaks related to tortuosity and inadequate overlap and fixation.

The primary graft patency rate was no different from the surgical control group and no different from that reported by others.[19] It should be borne in mind that the results of stent grafting for aneurysms may be device specific. We did not compare the AneuRx device against other devices. Many are undergoing development and clinical investigation. Each will need to be compared with a suitable surgical control group.

In conclusion, endovascular stent graft repair of infrarenal aortic aneurysms compared favorably with open surgery with a significant reduction in patient morbidity and a significant reduction in hospital stay. The primary technical success rate was reduced in the stent graft group primarily as a result of incomplete aneurysm exclusion in 21% of patients at the time of discharge. However, at 30 days, there was no difference in primary or secondary procedural success rate and there was no difference in graft patency rate. Endoleak rate at 1 month and 6 months was 9% and at 12 months was 6%. Reliable long-term data are not yet available. There have been no aneurysm ruptures or conversions to open surgery.

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REFERENCES

1. Ernst CB. Abdominal aortic aneurysm. N Engl J Med 1993;328:1167-72.
2. Bengtsson J, Bergqvist D, Sternby NH. Increasing prevalence of abdominal aortic aneurysms: a necropsy study. Eur J Surg 1992;158:11-23.
3. Ouriel K, Green RM, Donayre C, Shortell CK, Elliott J, DeWeese JA. An evaluation of new methods of expressing aortic aneurysm size: relationship to rupture. J Vasc Surg 1992;15:12-20.
4. Johnansson G, Nydahl S, Olofsson P, et al. Survival of patients with abdominal aortic aneurysms: comparison between operative and non operative management. Eur J Vasc Surg 1990;4:497-502.
5. Nevitt MP, Ballard DJ, Hallett JW. Prognosis of abdominal aortic aneurysms: a population based study. N Engl J Med 1989;321:1009-14.
6. Reigel MM, Hollier LH, Kazmier FJ, O'Brien PC, Pairolero PC, Cherry KJ Jr, et al. Late survival in abdominal aortic aneurysm patients: the role of selective myocardial revascularization on the basis of clinical symptoms. J Vasc Surg 1987;5:222-8.
7. Bernstein EF, Dilley RB, Randolph HF, et al. The improving long term outlook for patients over 70 years of age with abdominal aortic aneurysms. Ann Surg 1988;207:318-22.
8. Golden MA, Whittemore AD, Donaldson MC, et al. Selective evaluation and management of coronary artery disease in patients undergoing repair of abdominal aortic aneurysms: a 16 year experience. Ann Surg 1990;212:415-23.
9. Cambria RP, Brewster DC, Abbott WM, L'Italien GJ, Megerman JJ, LaMuraglia GM, et al. The impact of selective use of dipyridamole-thallium scans and surgical factors on the current morbidity of aortic surgery. J Vasc Surg 1992;15:43-50.
10. Johnston KW. Multicenter prospective study of nonruptured abdominal aortic aneurysm. Part II: variables predicting morbidity and mortality. J Vasc Surg 1989;9:437-47.
11. Parodi JC, Palmaz JC, Barone HD. Transfemoral intraluminal graft implantation for abdominal aortic aneurysms. Ann Vasc Surg 1991;5:491-9.
12. Moore WS, Rutherford RB. Transfemoral endovascular repair of abdominal aortic aneurysm: results of the North American EVT phase 1 trial. J Vasc Surg 1996;23:543-53.
13. White GH, Yu W, May J, et al. Three-year experience with the White-Yu endovascular GAD graft for transluminal repair of aortic and iliac aneurysms. J Endovasc Surg 1997;4:124-36.
14. Blum U, Langer M, Spillner G, et al. Abdominal aortic aneurysms: preliminary technical and clinical results with transfemoral placement of endovascular self-expanding stent-grafts. Radiology 1996;198:25-31.
15. May J, White GH, Yu W, Waugh RC, Stephen MS, McGahan T, et al. Surgical management of complications following endoluminal grafting of abdominal aortic aneurysms. Eur J Vasc Endovasc Surg 1995;10:51-9.
16. Chuter TAM, Wendt G, Hopkinson BR, et al. Transfemoral insertion of a bifurcated endovascular graft for aortic aneurysm repair: the first 22 patients. J Cardiovasc Surg 1995;3:121-8.
17. Mialhe C, Amicabile C, Becquemin JP. Endovascular treatment of infrarenal abdominal aneurysms by the Stentor system: preliminary results of 79 cases. J Vasc Surg 1997;26:199-209.
18. Blum U, Voshage G, Lammer J, et al. Endoluminal stent-grafts for infrarenal abdominal aortic aneurysms. N Engl J Med 1997;336:13-20.
19. Allen RC, Fogarty TJ. The Medtronic-AneuRx modular bifurcated graft. In: Yao JST, Pearce WH, editors. Techniques in vascular and endovascular surgery. Stamford (CT): Appleton and Lange; 1998. p. 401-9.
20. White RA, Donayre CE, Walot I, Kopchok GE, Wilson E, Heilbron M, et al. Modular bifurcation endoprosthesis for treatment of abdominal aortic aneurysms. Ann Surg 1997; 226:381-9.
21. May J, White GH, Yu W, Ly CN, Waugh R, Stephen MS, et al. Concurrent comparison of endoluminal versus open repair in

the treatment of abdominal aortic aneurysms: analysis of 303 patients by life table method. J Vasc Surg 1998;27:213-21.
22. Allen RC, White RA, Zarins CK, Fogarty TJ. What are the characteristics of the ideal endovascular graft for abdominal aortic aneurysm exclusion? J Endovasc Surg 1997;4:195-202.
23. Richardson JD, Main KA. Repair of abdominal aortic aneurysms. A statewide experience. Arch Surg 1991;126: 614-6.
24. Ahn SS, Rutherford RB, Becker GJ, Comerota AJ, Johnston KW, McClean GK, et al. Reporting standards for lower extremity arterial endovascular procedures. J Vasc Surg 1993;17:1103-7.
25. Perry MO, Calcagno D. Abdominal aortic aneurysm surgery: the basic evaluation of cardiac risk. Ann Surg 1988;208:738-42.
26. Johnston KW, Canadian Society for Vascular Surgery Aneurysm Study Group. Nonruptured abdominal aortic aneurysm: six-year follow-up results from the multicenter prospective Canadian aneurysm study. J Vasc Surg 1994;20:163-70.
27. AbuRahma AF, Robinson PA, Boland JP, et al. Elective resection of 332 abdominal aortic aneurysms in a southern West Virginia community during a recent 5 year period. Surgery 1991;109:224-51.
28. Wen SW, Simunovic M, Williams JI, et al. Hospital volume, calendar age, and short term outcomes in patients undergoing repair of abdominal aortic aneurysms; the Ontario experience, 1988-92. J Epidemiol Community Health 1996; 50:207-13.
29. Katz DJ, Stanley JC, Zelenock GB. Operative mortality rates for intact and ruptured abdominal aortic aneurysms in Michigan: an eleven-year statewide experience. J Vasc Surg 1994;19:804-17.
30. Kazmers A, Jacobs L, Perkins A, Lindenauer SM, Bates E. Abdominal aortic aneurysm repair in Veterans Affairs medical centers. J Vasc Surg 1996;23:191-200.
31. Zarins CK, Harris EJ Jr. Operative repair for aortic aneurysms: the gold standard. J Endovasc Surg 1997;4:232-41.
32. Hannan EL, Kilburn H, O'Donnell JF, et al. A longitudinal analysis of the relationship between in-hospital mortality in New York State and the volume of abdominal aortic surgeries performed. Health Serv Res 1992;27:517-42.
33. North American Symptomatic Carotid Endarterectomy Trial Collaborators. Beneficial effect of carotid endarterectomy in symptomatic patients with high-grade carotid stenosis. N Engl J Med 1991;325:445-53.
34. Executive Committee for the Asymptomatic Carotid Atherosclerosis Study. Endarterectomy for asymptomatic carotid artery stenosis. JAMA 1995;273:1421-8.
35. Zarins CK. Carotid endarterectomy: the gold standard. J Endovasc Surg 1996;3:10-5.
36. Lumsden AB, Allen RC, Chaikof EL, et al. Delayed rupture of aortic aneurysms following endovascular stent grafting. Am J Surg 1995;170:174-8.
37. Parodi JC. Endovascular repair of abdominal aortic aneurysms and other arterial lesions. J Vasc Surg 1995; 21:549-57.
38. Blum W, Voshage G, Beyersdorf F, Tollner D, Spillner G, Morgenroth A, et al. Two-center German experience with aortic endografting. J Endovasc Surg 1997;4:137-46.
39. Chuter TAM, Risberg B, Hopkinson BR, Wendt G, Scott RAP, Walker PJ, et al. Clinical experience with a bifurcated endovascular graft for abdominal aortic aneurysm repair. J Vasc Surg 1996;24:655-66.
40. Kretschmer G, Holzenbein T, Lammer J, Thurnher S, Minar E, Polterauer P. The first 15 months of transluminal abdominal aortic aneurysm management: a single centre experience. Eur J Vasc Endovasc Surg 1997;14:24-32.
41. May J, White GH, Yu W, Waugh R, Stephen M, Sieunarine K, et al. Conversion from endoluminal to open repair of abdominal aortic aneurysms: a hazardous procedure. Eur J Vasc Endovasc Surg 1997;14:4-11.
42. White RA, Donayre CE, Walot I, Kopchok GE, de Virgilio C, Mehringer CM. Aortic aneurysm morphology for planning endovascular procedures. Tex Heart Inst J 1997; 24:160-6.

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APPENDIX. CLINICAL INVESTIGATION SITES

Institution	*Principle investigator*	*Coinvestigators*	*Study coordinator*
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Surgical Care Associates (Louisville, Ky)	Edward Kinney, MD	None	Shannon Buckman, RN (502-897-5139)
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DISCUSSION

Dr Michael S. Makaroun (Pittsburgh, Pa). Dr Zarins and his colleagues have presented the results of a second well-designed and well-controlled prospective trial comparing open surgical repair to stent graft repair of abdominal aortic aneurysms. The outcomes support the conclusion that, in a carefully selected group of patients with aneurysmal disease, endovascular repair can achieve total exclusion of the aneurysm with acceptable mortality, morbidity, and failure rates. Short-term benefits include reduced blood loss, decreased hospital stay, and an earlier recovery. It is encouraging to note that the results of phase II are better than phase I, despite initiating eight additional sites. This suggests that lessons learned with the early experience of a new device can effectively be transferred to new users with the avoidance of a steep learning curve at each site. This should be welcome news to everybody in this audience.

Dr Zarins, I have a few questions for you.

We recently presented to the Society for Clinical Vascular Surgery in March of this year our personal experience with the first 50 endovascular repairs that we performed, and we compared them to our concurrent surgical patients. The main advantage of endovascular repair in our experience was reduced blood loss and shorter hospital stay with no major difference in morbidity. In your comparison to open procedures, medical complications were notably reduced in the stent graft group. However, the most severe medical complications that resulted in five deaths in your stent graft group are not included in this comparison. If these were included, would the benefits still be apparent?

The numbers of reoperations in your open surgical patients were significantly higher than in the stent graft group. However, a 10% reoperation rate and a 5% multiple reoperation rate is much higher than expected. Our rate is less than 3%, and, in the EVT trial that was presented earlier today, the rate was around 1%. Was this a chance occurrence because of a small sample size in the open surgical group, or is this the experience with all open cases at the 12 institutions in this study?

My second question relates to the endoleaks that remain a major problem with this new technique and that result in aneurysm enlargement and several reported ruptures. A third of your patients with a leak at 6 months had a decreased aneurysm size, which is quite different from many reports, including our own experience. How do you explain this apparent regression of the aneurysm in the face of the persistent leak? And do you feel comfortable following patients expectantly when they have a leak and no reduction in size of the aneurysm?

With three cases of migration in a short-term follow-up period and the known propensity of the remaining neck to dilate, do you feel there is any benefit or need for a more secure attachment of the device to the neck of the aneurysm as compared with the present device that you are using?

Finally, with a mortality rate of 2.6% and a total complication rate of 17%, would you recommend the use of this technique for small aneurysms, especially in the 3-cm to 4-cm range as allowed in your protocol?

I would like to congratulate the authors on their excellent results in the stent graft repair. There should be no residual doubt that endovascular repair of aneurysms is here to stay and that improved results can be expected with improving technology. I enjoyed your presentation and the opportunity to review the manuscript, and I thank the Society for the privilege of discussing it.

Dr Christopher K. Zarins. Thank you, Dr Makaroun, for your discussion.

With regards to your first question regarding the medical morbidity and mortality rates, in calculating our results we counted each patient's outcome according to the most severe event so that we would not duplicate counting events. So, if a patient had a major medical complication and died, that patient was counted as a death as opposed to a major medical complication. Similarly, if a patient had a major surgical complication and also a medical complication, he was counted as a major surgical complication. The patient in the surgical group with a 74-day hospital stay had multiple reoperations and multiple medical complications but was counted once as a surgical complication. So, in that you are correct—if we counted each medical complication individually, the rate would be higher in both the stent graft and surgical group. But the overall benefit of reduced morbidity in the stent graft group remains.

You noted that the reoperation rate in the surgical group was higher than at your institution, and I might add that it is higher than at my institution as well. However, it is important to note that this is a multicenter prospective clinical trial and that such trials generally have outcomes that are not as good as those reported by single institutions. You may recall that the stroke/death rate for carotid endarterectomy in the North American Symptomatic Carotid Endarterectomy Trial and the Asymptomatic Carotid Atherosclerosis Study were higher than those found in most large published series of carotid endarterectomy. It is possible that the reoperation rate for stent graft repair of aneurysms as reported in this trial is also higher than you experience at your institution. The important measure in a multicenter trial is the comparison of the end points between the two study groups. In this study, the complications were counted in the same manner in both groups, and clearly there were fewer complications in the stent graft group.

The endoleak question is an important question. We obviously need to pay attention to the 9% endoleak rate at 6 months. A significant number of those aneurysms did become smaller as you noted, and I do not have a ready explanation. Perhaps it is because the endoleaks are small as related to lumbar arteries. The outcome and the ultimate significance of those small endoleaks remains to be determined. Large endoleaks or cases in which the aneurysm enlarges should be treated promptly. The modular design of this stent graft system allows the insertion of proximal and distal extender cuffs to seal junctional leaks.

In response to your question on migration, I should note that the migrations we observed were never in a longitudinal direction because of the longitudinal columnar support in this device. Migrations were in a lateral sense, such as in the case that I showed. Two were proximal leaks, and they were corrected with proximal extender cuffs. I think they were related to short necks and tortuous necks. As we become more skilled at precisely localizing the stent graft immediately at the renal arteries, perhaps we will see fewer of these in the future. The third migration was a result of a low placement of the iliac limbs in the bifurcation segment junction. This was corrected with an extender cuff to cover that junction site. So I do not know whether migration does in fact occur. I share your concern of possible future dilation of the infrarenal neck, and this is something that we need to look for and monitor over time.

As far as the mortality rate and whether we should be treating small aneurysms is concerned, I will note that the mortality rate in the 150 patients in phase II was 1.3%. I think that patients who undergo stent graft repair now tend to be older and sicker and more frail than we have seen for open surgical repair. Thus, I am not sure you can evaluate these devices primarily on the basis of the mortality rate because the mortality rate to a large extent may be caused by patient comorbidities rather than by the procedure. With regard to the question of small aneurysms, we do see patients with small aneurysms who are requesting these procedures. Thus far, the data supports their use for small aneurysms, but clearly more data and longer follow-up periods are needed to satisfactorily answer this question.

Dr Samuel S. Ahn (Los Angeles, Calif). This was an excellent presentation, and I congratulate you for those encouraging results. I just have a series of related questions. One, did you keep track of the patients who were excluded? If so, how many patients were excluded or what percentage were excluded? And third, what can we do to improve the inclusion criteria?

Dr Zarins. We have evaluated a large number of patients, but we have not specifically tracked patients who were excluded. I would guess that our overall acceptance rate is about 50% to 60% of patients who present with abdominal aortic aneurysms, but it may be higher. We certainly need to track all patients with aneurysms as you suggest to fully evaluate this procedure.

Dr William J. Quinones-Baldrich (Los Angeles, Calif). I also want to congratulate you on your excellent

results and a nice presentation. One of the observations that has been made recently has been that as aneurysms shrink in diameter they also shrink in length. In one of the European society papers, the shortening in length is actually greater than the change in diameter. My question relates to the incidence of migration that you observed and whether or not you feel that this may be related to the fact that your device is fully supported and may not be able to accommodate the shrinking in the length of the aneurysm.

Dr Zarins. You have made a good point that needs to be carefully studied. In our three cases of migration, we have seen elongation with the appearance of a late endoleak rather than shrinkage in length and have corrected the problem with increasing the length with extender cuffs. Your concern, of course, is that if the aneurysm shrinks in length, it possibly might move the stent graft to cover a renal artery. We have not encountered this and have seen no evidence of longitudinal migration. However, it is something that we will need to watch for and observe.

Dr Geoffrey M. White (Sydney, Australia). I would like to ask a brief question about the incidence of primary endoleaks in this trial. To date, we have used the Medtronic graft in 23 cases and have documented a 43% incidence rate of endoleak on contrast enhanced computed tomographic scans performed before discharge. Most of these endoleaks appeared to be through small defects in the graft wall.

You have reported a 21% endoleak rate at discharge, with a much lower incidence rate of endoleak at 6 months and 12 months follow-up. Therefore, it would be reasonable to presume that many of the endoleaks have closed by a process of thrombosis over the interval of 6 or 12 months of follow-up. I would like to hear your opinion regarding the safety of a thrombotic seal for closure of an endoleak through a small defect in the graft wall and your thoughts concerning the long-term behavior of such sealed endoleaks.

Dr Zarins. The endoleak rate before discharge was 27% in our experience, and we thought that 10 of those patients had transgraft flow, which is the occurrence of small openings in the polyester graft made by the needle used to suture it to the nitinol stent. Those leaks uniformly seal. I do not think that those will be a problem. I think that of more concern are persistent leaks related to attachment sites or to branch flow. I do not think that the transgraft flow will be a major problem.